with a notable recent increase in utilization for Severe Aplastic Anemia (SAA). Recent data, although limited, has suggested that unrelated cord blood transplantation can be a successful treatment strategy for patients with SAA lacking a well-matched adult donor. A retrospective analysis was performed as a means to compare the SLCBB experience (n = 42) with published results. Outcomes data was available and evaluated for 16 singleton cord transplants. This population included 11 pediatric and 5 adult patients. The mean age was 15.4 years (1.7-45.2). Donor/recipient HLA matching was six of six (n = 2), five of six (n = 8), four of six (n = 6). Median total nucleated cell dose was 7.2×10^7/kg. Fourteen patients received myeloablative conditioning regimens while two received non-myeloablative conditioning. Thirteen patients achieved neutrophil engraftment with a median time to recovery of 21 days (9-46). The six patients who received a total nucleated cell dose (TNC) $> 5.0 \times 10^7$/kg had a median time to engraftment of 20 days as compared to 27 days for patients receiving a TNC dose $< 5.0 \times 10^7$/kg. There was one instance of graft failure and one patient censored due to early death. Ten patients are alive and three have expired from infectious complications. Acute GVHD occurred in nine patients and chronic GVHD developed in six. Outcomes for dual cord transplants (n = 11) were available for three patients. All three patients engrafted with a median time to absolute neutrophil recovery of 25 days (22-28). These findings support that unrelated cord blood transplant is a feasible treatment strategy for Severe Aplastic Anemia. The SLCBB will continue to track and report outcomes for this population.

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOFIBROSIS – CLOSE POST-TRANSPLANT SURVEILLANCE IS MANDATORY

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Introduction: Primary and post-ET/PV-myelofibrosis (MF) is a rare myeloproliferative disorder with a very variable, on the long term always fatal course. After allogeneic hematopoietic cell transplantation (alloHCT) encouraging short term survival has been reported. We present data from 57 consecutive transplants for MF in our institution, demonstrating that close monitoring of the post-transplant course is warranted.

Methods: Between 2000 and 2009 40 males and 17 females with primary MF (n = 48) and MF post ET or PV (n = 9) were grafted with unmanipulated bone marrow (n = 22) or peripheral stem cells (n = 35) from a related (n = 14) or an unrelated (n = 43) donor. Median (md) age was 54 (19-68) years. Fifteen patients (pts) had low, 28 intermediate and 14 high risk disease (Dupriez score 0, 1, 2). Karyotype was favorable in 35, unfavorable in 16 and unsuccessful in 6 pts. All but four pts received intermediate intensity conditioning (TBI(8 Gy)/Flud/Cy n = 29 or Bu(10)/Flud n = 24, standard n = 4). In all except 4 matched transplants rabbit ATG was added before grafting.

Results: All pts engrafted at a md of 25 (11-70) days. 16 pts either transiently or permanently lost complete chimerism during follow up with proven relapse at a md of 376 (69 – 1211) days in 12. Overall probability of relapse at 4 years is 32%. At a md follow up of 46 (4-115) months probability of overall versus relapse free survival (RFS) is 66% vs 50% for the whole cohort. Probability of RFS is significantly less in pts with unfavorable karyotype compared to those with favorable karyotype (21 vs 63%, p = 0.004) and for pts with circulating blasts > 1% compared to those with blasts < = 1% (27 vs 61%, p = 0.002). Twelve pts with decreasing chimerism/relapse received immunotherapy (6 PBSC boosts, 8 donor lymphocyte infusions) with 8 patients responding. In 6 pts response was complete, 2 subsequently lost their response and 5 ultimately had to receive a second transplant

Conclusions: Our results underscore the need for closely monitoring MF pts after alloHCT. Problems with loss of donor chimerism and relapse post-transplant are common however may well respond to cellular immunotherapy. For full evaluation of the role of alloHCT in the management of MF long term results are warranted.

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ADDITION OF BUSULFAN TO FLUDARABINE AND TOTAL BODY IRRADIATION CONDITIONED ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION ENHANCES DONOR T-CELL ENGRAFTMENT AND OPTIMIZES DISEASE CONTROL

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While nonmyeloablative allogeneic hematopoietic stem cell transplantation (HSCT) is associated with a reduction in treatment associated toxicity, limitations in disease control continue to impact overall outcomes. Key to optimizing disease remission is the rapid integration of the donor T cell compartment to maximize graft vs. malignancy activity. While details on the kinetics of engraftment in nonmyeloablative HSCT is limited, reports by two groups (Baron F. et al, Blood, 2004,104:2254 and Saito B. et al, BBMT, 2008 14:1148) concur that low donor T-cell chimerisms by Day +30 portend poorer outcomes from either disease progression or engraftment failure. Therefore, manipulation of the transplant procedure to optimize engraftment outcomes early in the post-transplant course is vital to maximize outcomes. To this end, we established an institutional reduced-intensity regimen of busulfan 3.2 mg/kg IV, fludarabine 90 mg/m^2 and TBI 2 Gy followed by allogeneic peripheral blood stem cell transplant. Our GVHD prophylaxis regimen includes cyclosporine and MMF. This report describes our early T cell chimerism data in 76 patients and shows a correlation between T cell chimerism and disease control.

The mean percentage of donor CD3+ cells was 72% at Day +28, 98% at Day +56 and 99.9% at Day +84, which compare favorably to previous reports of engraftment with fludarabine and TBI alone. We further analyzed chimerism data in those patients with measurable disease going into transplant and those with early relapse despite remission at the time of transplant. In 13 patients that were not in complete remission at the time of transplant, but subsequently achieved complete remission, the mean CD3+ donor cells at Day +28 was 85% and 92% at Day +56. This is in stark contrast to the group of 7 patients who were in complete remission at the time of transplant, but rapidly relapsed post-transplant, with a mean Day +28 CD3+ donor cells of 57%, with minimal improvement to an average of 63% at Day +56, statistically significantly different from the group achieving remission. Additional findings with this regimen include 2 year survival of 49%, with acceptable levels of GVHD.

The addition of busulfan to the backbone of fludarabine and TBI enhances early T cell engraftment, leading to optimal disease control by harnessing graft vs. malignancy activity. Early poor T cell chimerisms may define those at high-risk of relapse, prompting interventions to enrich donor T cell constitution.

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TARGETED IV BUSULFAN AND FLUDARABINE FOLLOWED BY POST-ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION RITUXIMAB DEMONSTRATE ENCOURAGING ACTIVITY IN HIGH RISK CD20 + POSITIVE LYMPHOID MALIGNANCIES WITHOUT INCREASED INFECTIOUS COMPLICATIONS

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Rituximab has activity in lymphoid malignancies and may augment responses after allogeneic hematopoietic cell transplantation (HCT); however prolonged lymphopenia may increase the risk for infectious complications. We examined the safety of Rituximab after reduced toxicity conditioning HCT. Sixteen patients (median age 56, range 35 – 68), (CLL 7, follicular lymphoma 4, mantle cell lymphoma3, and large cell lymphoma 2 with CD20 positive lymphoid malignancies. Twelve had a partial response and 4 complete

response to prior conditioning with pharmacokinetic-targeted IV busulfan(130-145 mg/m2) and fludarabine (40 mg/m^2) x 4 days (t-IV Bu/Flu) followed by HCT. All were treated with rituximab at 375 mg/m2 on days 1 and 8 after a matched related (n = 7), mismatched related (n = 1), matched unrelated(n = 6), or mismatched unrelated (n = 2) HCT. Two patients received ATG as GVHD prophylaxis. Median time to neutrophil and platelet engraftment was 15 and 13 days, respectively. Maximum grades of aGVHD observed were 0 (n = 4), 1(n = 7), 2 (n = 7), and 3 (n = 1). Moderate/severe cGVHD occurred in only 3/16. With a median F/U of 15 months (range: 2-33), complete response was achieved in 12, persistent residual disease in 3, and progressive disease in 1. CMV reactivation(n = 8), as well as bacterial (n = 8), fungal (n = 3), and viral (n = 3) infection did not appear to exceed historical rates without rituximab. After HCT, prolonged lymphopenia was demonstrated: Median absolute lymphocyte counts (0.84 K/uL) remained below the reference range through one year. In 5/16 subjects for which B-cell data was available, B-cell lymphopenia persisted to one year after HCT. The addition of rituximab 375 mg/m^2 to t-IV Bu/Flu followed by allogeneic HCT has encouraging activity in the treatment of lymphoid malignancies. While both absolute and B-cell lymphopenia were observed through one year after HCT, infectious complications have not exceeded historical rates.

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THE INCIDENCE OF HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME (SOS) FOLLOWING A PREPARATIVE REGIMEN OF DOSE TARGETED INTRAVENOUS BUSULFAN AND CYTOXAN AND A GRAFT VERSUS HOST DISEASE PROPHYLACTIC REGIMEN OF TACROLIMUS AND METHOTREXATE: A SINGLE INSTITUTION EXPERIENCE

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Hepatic sinusoidal obstruction syndrome (SOS) is a common complication of preparative regimens in the setting of stem cell transplantation. The use of intravenous Busulfan (Bu), however, resulted in decrease in the incidence of SOS to 8%. The graft-versus-host-disease (GVHD) prophylactic regimen seems also to impact the risk of SOS following an ablative transplant. The goal of this study is to determine the incidence of clinically significant SOS in a homogenous cohort of patients who received an ablative regimen of dose targeted intravenous Busulfan and cytoxan (Bu/Cy), and received tacrolimus and methotrexate (Tac/MTX) for GVHD prophylaxis.

Methods: In this retrospective study, patients who received an ablative regimen of intravenous Bu/Cy, and received Tac/MTX for GVHD prophylaxis were identified. Data collected include: age, indication for transplant, disease status at transplant, stem cell source, date of transplant, date of onset of clinically significant SOS, and date and cause of death. Patients who underwent an ablative regimen of total body irradiation (TBI) and cytoxan and received the same GVHD prophylactic regimen were used for comparison.

Results: Between September, 2007 and August, 2009, 34 patients received an ablative regimen of intravenous Bu/Cy and GVHD prophylactic regimen of Tac/MTX. In this cohort, age ranged from 25 to 63 years old. Diagnoses were as follows: AML n = 20, MDS n = 7, CML n = 4, myelofibrosis n = 2, and NHL n = 1. Disease status at diagnosis was CR1 n = 16, ≥ CR2 n = 5, relapsed/refractory n = 2, untreated n = 6, PR n = 3, chronic phase CML n = 2. In this cohort, only three (8.8%) patients developed clinically significant SOS. Two patients were diagnosed within 3 weeks of transplant, however, one patient developed biopsy proven SOS 58 days post transplant. None of the patients in this cohort died of SOS. In 28 out of 34 patients, Bu pharmacokinetic (PK) studies were done properly. In two patients the Bu dose was increased and in one case the dose was decreased. In the comparison cohort, 29 patients received TBI/Cy conditioning regimen. In this cohort only one patient (3.4%) developed SOS.

Conclusion: The incidence of SOS in the cohort of patients who received dose targeted intravenous Bu/Cy and Tac/MTX for GVHD prophylaxis was comparable to the reported incidence of SOS in literature and appears to be higher than the incidence of SOS in the TBI/Cy and Tac/MTX cohort.

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COMORBIDITY SCORE IN ALLOGENEIC MYELOABLATIVE TRANSPLANTS CONDITIONED WITH FLUDARABINE/I.V. BUSULFAN (FLUBU4)

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The assessment of comorbidity score was previously demonstrated to predict the risk of transplant related mortality (TRM) in patients undergoing standard myeloablative allogeneic hematopoietic stem cell transplantation (HSCT). Since Flu/Bu4 regimen has been associated with limited extra-hematologic toxicity, we analyzed whether the comorbidity score may still represent a useful tool in transplant patients conditioned with this regimen. Of 52 consecutive patients who received a matched HSCT with FluBu4 at our institution, 50 were evaluable for assessing their pre-transplant comorbidity score according to the initial description (Sorror M et al. Blood 2005, 106:2912). The total dose of I.V. Bu was 12.8 mg/kg in 18 patients while in the remaining patients a targeted dose was given (AUC: 4800 μM*min). Patients were divided in three groups: group A, score 0 (n = 8); group B, score 1-2 (n = 16), group C, score ≥ 3 (n = 26). The three groups did not differ significantly in age, diagnosis, previous lines of chemotherapy, type of donor and targeted vs standard dose of I.V. Bu. Patients with active acute leukemia at the time of HSCT were 12% in group A, 18% in group B and 29% in group C (p = ns). Thirteen patients (26%) died due to relapse of their malignancy and 11 (22%) due to transplant-related complications. TRM was 12% in group A, 37% in group B and 15% in group C despite the fact that the rate of acute GVHD grade II-IV was slightly higher in group C (34%), compared to groups A (12%) and B (31%). Patients in group C had a trend for higher relapse-related mortality, 38%, compared to 12% observed in each of the other groups (p = 0.07). After a median follow-up of 640 days (range: 111-2065), a greater number of patients were alive and in remission in group A (75%) (p = 0.04), compared to group B (50%) and C (34%). In conclusion, a higher comorbidity score correlated with worse overall survival largely due to increased relapse. However, it did not predict TRM in patients conditioned with FluBu4.

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CHILDREN WITH ACUTE LEUKEMIA: A COMPARISON OF OUTCOMES FROM ALLOGENEIC BLOOD STEM CELL AND BONE MARROW TRANSPLANTATION

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The relative merits of PBSCT versus BMT for children with standard and high risk hematologic malignancies remain unclear. In a retrospective single center study, we compared allogeneic peripheral blood stem cell transplantation (PBSCT) (n = 30) with bone marrow transplantation (BMT) (n = 110) in children with acute leukemia between January 1st, 2001 and September 30th, 2006. Four (13.3%) PBSCT patients received HLA identical sibling donors versus 38 (34.5%) who received marrow: 15 (50.0%) PBSCT recipients received HLA mismatched PBSC versus 10 (9.1%) receiving marrow. Nine (30.0%) PBSCT patients had an HLA matched unrelated donor versus 49 (44.5%) of marrow recipients. Two PBSCT (6.7%) were from mismatched unrelated donors versus 13 (11.8%) in the marrow recipients. The median age for PBSCT was 9 years versus 8 years for BMT. Descriptive statistics were used to summarize the demographic and medical variables. The unadjusted probabilities of disease-free survival were estimated using the Kaplan-Meier method. The association of graft-source and time to each of the study endpoints was estimated by Cox's regression model and the occurrence of GvHD was included as a time-dependent covariate. Time to both neutrophil engraftment and platelet independence